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Safety of *Schizochytrium* sp. oil as a novel food pursuant to Regulation (EU) 2015/2283

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Abstract

Following a request from the European Commission, the EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA) was asked to deliver an opinion on the safety of *Schizochytrium* sp. oil as a novel food (NF) pursuant to Regulation (EU) 2015/2283. *Schizochytrium* sp. is a single-cell microalga. The strain WZU477, used by the applicant (Progress Biotech bv), was found to belong to the species *Schizochytrium limacinum* and was obtained in a marine environment from rotted mangrove forest leaves. The NF, an oil rich in docosahexaenoic acid (DHA), is isolated from the microalgae by mechanical extraction. The applicant proposed to use the NF in infant formulae (IF) and follow-on formulae (FOF). The use level defined by the applicant was derived from Regulation (EU) 2016/127, which states the mandatory addition of DHA to IF and FOF at the level of 20–50 mg/100 kcal. The intake of DHA resulting from the use of the NF in IF and FOF is not expected to pose safety concerns. The composition of the NF indicates the absence of marine biotoxins in the NF. Furthermore, *Schizochytrium limacinum* was attributed the qualified presumption of safety (QPS) status with the qualification 'for production purposes only'. Based on the information provided, the microalga is not expected to survive the manufacturing process. Toxicological tests conducted with the NF were not performed. However, based on the available toxicological data on various forms of oils derived from *Schizochytrium* sp., the QPS status of the source of the NF, the production process and the composition of the NF, the Panel considers there are no concerns with regard to toxicity of the NF. The Panel concludes that the NF is safe under the proposed conditions of use.

Keywords: Novel foods, *Schizochytrium limacinum*, docosahexaenoic acid (DHA), infant and young children, alga, fatty acid, safety

Requestor: European Commission

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

Schizochytrium sp. oil is authorised, in accordance with Regulation (EC) No 258/97[1], as a novel food for a number of uses as listed in Commission Implementing Regulation (EU) 2017/2470[2] establishing the Union list of novel foods in accordance with Regulation (EU) 2015/2283[3].

On 14 March 2019, the company Progress Biotech bv submitted a request to the European Commission in accordance with Article 10 of Regulation (EU) 2015/2283 for an extension of use of *Schizochytrium* sp. oil as a novel food. The applicant requests to extend the use of *Schizochytrium* sp. oil to additional food categories, namely, infant formulae, follow-on formulae and fruit/vegetable puree. The applicant has also requested data protection under Article 26 of Regulation (EU) 2015/2283.

In accordance with Article 10(3) of Regulation (EU) 2015/2283, the European Commission asks the European Food Safety Authority to provide a scientific opinion on *Schizochytrium* sp. oil.

1.2. Interpretation of the Terms of Reference

The request of the European Commission is to provide a scientific opinion on the extension of use for the NF *Schizochytrium sp*. oil (already authorised). Therefore, it was the interpretation of the Panel that only new uses requested by the applicant shall be assessed in the present opinion. It was noted by the Commission and by the Panel that the use of the NF in fruit/vegetable puree (100 mg/100 g) was already authorised. Therefore, this use was not assessed in the present opinion. Only the uses in infant formulae and follow-on formulae were assessed.

1.3. Information on existing evaluations and authorisations

Five existing evaluations of the NDA Panel of EFSA need to be mentioned:

- In the Scientific Opinion on Dietary Reference Values for fats (EFSA NDA Panel, 2010), the NDA Panel set an adequate intake (AI) of 250 mg for eicosapentaenoic acid (EPA) plus docosahexaenoic acid (DHA) for adults; an AI of 100 mg DHA for infants (> 6 months) and young children < 24 months; and increased by 100–200 mg preformed DHA in addition to the AI for adults as an adequate supply of n-3 long-chain PUFA during pregnancy and lactation.
- In the Scientific Opinion related to the tolerable upper intake level of eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and docosapentaenoic acid (DPA) (EFSA NDA Panel, 2012), the Panel concluded that a tolerable upper intake level for DHA could not be established. However, it was demonstrated that supplemental intakes of EPA and DHA combined at doses up to 5 g/day, and supplemental intakes of EPA alone up to 1.8 g/day, do not raise safety concerns for the adult population. The Panel also considered that supplemental intakes of DHA alone up to about 1 g/day do not raise safety concerns for the general population. Limited data were available on the effects of long-term supplementation with DHA alone at higher doses.
- In the Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union (EFSA NDA Panel, 2013), the Panel concluded on the levels of nutrient and energy intakes that are considered adequate for the majority of infants and young children. In particular, the adequate intake for DHA of 100 mg/day was confirmed for infants and young children between 6 and 24 months and was also applied to infants in the period 0–6 months, taking into account the concentration of essential fatty acids (including DHA) in human breast milk. It is noted that there is no AI for DHA set for children after 24 months.
- In the Scientific Opinion on the essential composition of infant and follow-on formulae (EFSA NDA Panel, 2014a), the Panel concluded that DHA should be added to infant formulae (IF) and follow-on formulae (FOF) due to its structural role in the nervous tissue and the retina and its

[1] Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel foods ingredients. OJ L 43, 14.2.1997, p. 1.
[2] Commission Implementing Regulation (EU) 2017/2470 of 20 December 2017 establishing the Union list of novel foods in accordance with Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods. OJ L 351,30.12.2017, p. 72.
[3] Regulation (EU) 2015/2283 of the European Parliament and of the Council of 25 November 2015 on novel foods, amending Regulation (EU) No 1169/2011 of the European Parliament and of the Council and repealing Regulation (EC) No 258/97 of the European Parliament and of the Council and Commission Regulation (EC) No 1852/2001. OJ L 327, 11.12.2015, p. 1.

involvement in normal brain and visual development, the need of the developing brain to accumulate large amounts of DHA in the first 2 years of life and the consideration that the intake of preformed DHA generally results in an erythrocyte DHA status more closely resembling that of a breast-fed infant than is achieved with alpha linolenic acid (ALA) alone. A range for the recommended concentration of DHA in IF and FOF was derived: from 20 mg/100 kcal (4.8 mg/100 kJ), based on the adequate intake of DHA (100 mg/day) and an average energy intake of 500 kcal/day, to 50 mg/100 kcal (12 mg/100 kJ), based on the highest observed DHA concentration in human milk (1% DHA in fatty acids (FAs) and the amount of FA in human milk).

- In the Scientific Opinion on the extension of use for DHA and EPA-rich algal oil from *Schizochytrium* sp. as a NF ingredient (EFSA NDA Panel, 2014b), it was concluded that the use of the NF in food supplements up to a maximum DHA and EPA content of 3 g per daily dose for the adult population, excluding pregnant and lactating women, was safe for the consumer.

2. Data and methodologies

2.1. Data

The safety assessment of this NF is based on data supplied in the application and information submitted by the applicant following EFSA requests for supplementary information. In addition, information provided by the EFSA Panel on Biological Hazards has also been considered (EFSA BIOHAZ Panel, 2020).

Administrative and scientific requirements for NF applications referred to in Article 10 of Regulation (EU) 2015/2283 are listed in the Commission Implementing Regulation (EU) 2017/2469[4].

A common and structured format on the presentation of NF applications is described in the EFSA Guidance on the preparation and presentation of an NF application.[5] As indicated in this Guidance, it is the duty of the applicant to provide all of the available (proprietary, confidential and published) scientific data, including both data in favour and not in favour to supporting the safety of the proposed NF.

This NF application includes a request for the protection of proprietary data.

2.2. Methodologies

The assessment follows the methodology set out in the EFSA Guidance on NF applications (EFSA NDA Panel, 2016) and the principles described in the relevant existing guidance documents from the EFSA Scientific Committee. The legal provisions for the assessment are laid down in Article 11 of Regulation (EU) 2015/2283 and in Article 7 of the Commission Implementing Regulation (EU) 2017/2469.

This assessment concerns only risks that might be associated with consumption of the NF under the proposed conditions of use and is not an assessment of the efficacy of the NF with regard to any claimed benefit.

3. Assessment

3.1. Introduction

The NF, which is the subject of the application, is the '*Schizochytrium* sp. oil'. It is produced by the microalgae *Schizochytrium* sp. (strain WZU477). With reference to article 3 of the NF Regulation 2015/2283, the NF falls under the category 2(a)(ii): 'food consisting of, isolated from or produced from microorganisms, fungi or algae'. The production process involves the controlled growth of this alga followed by the extraction and refinement of the oil produced by the algae. The oil is a mixture of triglycerides containing polyunsaturated fatty acids (PUFA) in which docosahexaenoic acid (DHA) represents more than 40% of total fatty acids. The NF is proposed to be used as an ingredient in infant formulae (IF) and follow-on formulae (FOF).

[4] Commission Implementing Regulation (EU) 2017/2469 of 20 December 2017 laying down administrative and scientific requirements for applications referred to in Article 10 of Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods. OJ L 351, 30.12.2017, pp. 64–71.

[5] EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), Turck D, Bresson J-L, Burlingame B, Dean T, Fairweather-Tait S, Heinonen M, Hirsch-Ernst KI, Mangelsdorf I, McArdle H, Naska A, Neuhäuser-Berthold M, Nowicka G, Pentieva K, Sanz Y, Siani A, Sjödin A, Stern M, Tomé D, Vinceti M, Willatts P, Engel K-H, Marchelli R, Pöting A, Poulsen M, Salminen S, Schlatter J, Arcella D, Gelbmann W, de Sesmaisons-Lecarré A, Verhagen H and van Loveren H, 2016. Guidance on the preparation and presentation of an application for authorisation of a novel food in the context of Regulation (EU) 2015/2283. EFSA Journal 2016;14(11):4594, 24 pp. https://doi.org/10.2903/j.efsa.2016.4594

3.2. Identity of the NF

The NF under assessment in the present application is an oil rich in docosahexaenoic acid (DHA). The usual names to define this NF are '*Schizochytrium* sp. oil', 'DHA-rich oil from *Schizochytrium*' or 'DHA-rich algal oil'. The oil produced by Progress Biotech bv is a formulation containing around 44% DHA.

The NF is isolated from marine microalgae belonging to the genus of *Schizochytrium*. The taxonomic classification of the microalgae is commonly defined as follows: Kingdom: Chromista; Phylum: Bigyra; Class: Labyrinthula; Order: Thraustochytriida; Family: Thraustochytriaceae; Genus: *Schizochytrium.*

Some databases refer to the taxonomy Eukaryota, stramenopiles instead of mentioning the Kingdom (Chromista) and the Phylum (Bigyra). Nevertheless, this is still leading to the class of Labyrinthula (https://www.uniprot.org/taxonomy/2163902). Furthermore, the taxonomic classification of the genus *Schizochytrium* has been subject to discussions in 2007 (Yokohama and Honda, 2007). Based on genetic and phenotypic analysis, the authors proposed changes in the classification. The genus *Schizochytrium* was amended and new genera like *Aurantiochytrium* and *Oblongichytrium* were defined. Therefore, the genus *Schizochytrium* can now also be referred to as *Aurantiochytrium*.

In the present application, it is specified that the strain 'WZU477' is used to produce the NF. The applicant clarified that this strain was obtained in a marine environment from rotted mangrove forest leaves. The strain *Schizochytrium* WZU477 is deposited at the China General Microbiological Culture Collection Centre under the reference number 1730 with an associated patent under the number 1916156 published by the Chinese patent office State Intellectual Property Office of the People's Republic of China (SIPO) in 2007. The strain WZU477 was selected without use of radiation, mutagenic agents or genetic modifications.

The identity of the strain WZU477 was addressed by the applicant based on the comparison of sequences of the 18S small subunit of ribosomal DNA (18S SSU-rDNA) gene. According to this analysis, the genetic sequence of the 18S rDNA gene of WZU477 presents 98% homology with the species *Schizochytrium limacinum* (based on 1,800 base pairs coding for 18S ribosomal RNA (rRNA)). In addition, the morphology of the cells observed using electron microscopy corroborates this conclusion. This information was previously assessed in the Netherlands by the Committee on Safety Assessment of Novel Foods (VNV Committee) (CBG-Meb, 2014), which concluded that the applicant had provided sufficient evidence to support the assumption that the strain WZU477 belongs to the species *Schizochytrium limacinum.* It is noted that *Schizochytrium limacinum* is a synonym of *Aurantiochytrium limacinum*.

3.3. Production process

The NF is produced according to the Food Safety System Certification (FSSC) 22000, which includes hazard analysis critical control points (HACCP) principles.

The unicellular microalgae *Schizochytrium* sp. (WZU477) are grown under controlled conditions (time, temperature, pH and aeration) in a liquid culture medium containing the necessary nutrients. The cultivation process starts in the laboratory. The production method and the control and verification processes ensure that the algae used in the production are pure cultures. The water used for the controlled growth of the microalgae and throughout the production process is food grade and conforms to food standard as required by ISO 22000. The applicant stated that the implemented steps ensure that the water does not contain any marine biotoxins or other compounds of concern for consumer safety. Quality control evaluations are performed at each stage of production in accordance with FSSC 22000 (which includes HACCP).

The microalgae cells are harvested from the liquid medium by centrifugation (on batch production basis). The harvested cells are immediately dried, and the oil is extracted. The cells lysis is carried out mechanically, using a high-pressure homogenising machine and a sand mill machine. The oil is subsequently concentrated by an additional centrifugation step to separate the oil fraction from the water and non-oil fraction. The crude oil is subsequently filtered and refined (decolouration and deodorisation using high temperature). At different steps of the process, authorised antioxidants are added to ensure stability. At final stage, the production process involves a standardisation step to reach the target concentration of DHA in the NF; a variable amount of 'high oleic sunflower oil' may therefore be added to the oil produced from the algae. The NF is finally packaged and stored at a temperature of –18°C.

Considering the high temperature and duration of certain steps of the production process (e.g. deodorisation and decolouration), viable cells are not expected to remain in the NF. The Panel considers that the microalga is not expected to survive the manufacturing process.

The Panel considers that the production process is sufficiently described and does not raise safety concerns.

The NF produced by the applicant is an oil which may undergo further processing steps (e.g. powdering) to be used as an ingredient of infant formulae and follow-on formulae. However, these steps are not carried out by the applicant, but by manufacturers of infant and follow-on formulae (see also Section 3.4.1 Stability of the NF under the intended conditions of use). Therefore, the description of the production process ends with the packaging and storing of the NF in its liquid/oily form.

3.4. Compositional data

The NF consists of triglycerides containing PUFA in which DHA is the predominant one.

In order to confirm that the manufacturing process is reproducible and adequate to produce a product with the required characteristics on a commercial scale, the applicant provided analytical information for six independent newly produced batches of the NF (40% Standard formulation) (**Tables 1a and 1b**). Information was provided on the accreditation of the laboratories that conducted the analyses presented in the application.

The proximate analytical results show that the NF is almost entirely composed of crude fat (98.7–99.7%). The remainder of the NF is composed of ash, moisture and volatiles. Levels of fibre and proteins in the NF are below the limit of quantification (LOQ) and the calculated carbohydrate content of the oil is below 1%.

The batch to batch analysis indicates a good repeatability of the production process. A slight variability of certain fatty acids (e.g. oleic acid ranging from 4.3% to 16.5% FA) was observed. This is explained by the use of a variable amount of 'high oleic sunflower oil' for the standardisation of the NF with respect to DHA. The DHA content in the NF (40.5–46.3% FA) is consistent through the six batches.

The composition of the NF can be compared to the composition of the two other NFs based on DHA-rich oil from *Schizochytrium* currently on the Union list and authorised for uses in IF and FOF: '*Schizochytrium* sp. (ATCC PTA-9695) oil' and '*Schizochytrium sp.* (T18) oil'. Compositional data for these NFs are available in the dossiers previously assessed by national authorities and submitted by DSM (2013) and Mara Renewable (2016). A comparison of the main long-chain (n-3) PUFA relevant in marine oils (DHA, EPA and DPA) was made. In the present NF, the average DHA content (44.2% of FA) is comparable to the DHA content of the two other NFs, which ranged between 37.1% and 44.4% of total FA. However, '*Schizochytrium sp.* (ATCC PTA-9695) oil' and '*Schizochytrium sp.* (T18) oil' contain higher levels of EPA (average 6 and 1.3% FA, respectively) compared to the oil from *Schizochytrium* WZU477 (average 0.56% FA). Regarding DPA (n-3), concentration is very low in the NF (0.1% FA), which is also the case in the two other NFs (< 1% FA).

Total sterol concentration varied between the different batches of the NF (3,470–5,097 mg/kg fat) but remains within the natural variation commonly observed in different types of oil (Yang et al., 2019). Furthermore, the concentration of sterols in the NF is lower than those measured in the authorised DHA oil from '*Schizochytrium* sp. (ATCC PTA-9695)' (5,100–5,600 mg/kg).

In terms of chemical contaminants and microbiological content, the composition of DHA oil from *Schizochytrium* WZU477 does not present any differences from '*Schizochytrium* sp. (ATCC PTA-9695) oil' and '*Schizochytrium* sp. (T18) oil'. The concentrations of metals (< LOQs), mycotoxins (< LOQ), polycyclic aromatic hydrocarbons (< LOQ), pesticide residues (< LOQ), PCBs, dioxins and glycidyl fatty acid esters found in this batch to batch analysis are within the EU limits established in the respective regulations and do not present concerns from a safety point of view. The concentrations of two contaminants (glycidyl fatty acid esters and 3-MCPD (3-monochloro-propanol-1,2-diol) fatty acid esters) exceeded the LOQ in two batches out of six. The refinement of the oil (including a deodorisation step at high temperature) can lead to the formation of such compounds in oils and these contaminants are currently regulated. For glycidyl fatty acid esters (expressed as glycidol), the maximum level (ML) in IF and FOF (liquid) is 6 μg/kg. For 3-MCPD (sum of 3-MCPD and 3-MCPD fatty acid esters, expressed as 3-MCPD), a draft regulation is close to adoption and will set an ML of 15 μg/kg in IF and FOF (liquid). The MLs for these contaminants are expected to be respected in the final product (IF and FOF) considering the incorporation rate of the NF in IF and FOF (max 87.5 mg NF/100 mL).

Upon request for additional data, the applicant provided analyses of common marine biotoxins in five independent batches of the NF (see **Table 1b**). These results indicate that marine biotoxins remain below the respective limits of quantification (LOQ) in all samples. These data confirm the assumption that the NF, produced from *Schizochytrium* sp. (strain WZU477), is not expected to contain marine biotoxins, neither produced by the source organism (for which a QPS status was concluded) nor from external contamination (considering the description of the production process in Section 3.3).

The Panel considers that the information provided on the composition of the NF is sufficient and does not raise safety concerns.

Table 1a: Batch to batch analysis of the NF (40% standard), PROXIMATE ANALYSIS and PHYSICO-CHEMICAL PARAMETERS

Parameter (unit)	Batch number					
	PB15232.3	PB16940715	NS-8107.2	PB19284.L	NS-9127	NS-9126
Proximate analysis						
Fat (g/100 g)	99.2	98.7	99.4	98.9	99.7	99.7
Proteins (g/100 g)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Carbohydrates (g/100 g)	< 1	< 1	< 1	< 1	< 1	< 1
Crude ash (g/100 g)	0.01	0.02	0.03	0.02	0.02	0.01
Crude fibre (g/100 g)	< 0.5	< 0.5	< 0.5	< 0.5	< 0.5	< 0.5
Physico-chemical parameters						
p-anisidine value	5.5[(a)]	5.9	4.3	2.9	2.6–2.8[(b)]	1.7–2.6[(b)]
Moisture & volatiles (%)	0.01	0.01	< 0.01	0.02	0.02	0.02
Unsaponifiable matter (%)	1.16	1.29	0.54	1.07	0.28	0.28
Acid value (mg KOH/g)	0.08	0.12	0.12	0.08	0.22–0.28[(b)]	0.14–0.28[(b)]
Peroxide value (meq/kg)	1[(a)]	0	0	0	0–4.8[(b)]	0–4.8[(b)]
Volumic mass (kg/L)	0.9318	0.936	0.935	0.9333	0.9344	0.9344

(a): For batch PB15232.3, p-anisidine value and peroxide value were measured by two different external labs in 2015 and 2020. The results obtained closest to production date (March 2015) were retained in the table, noting that higher results were found in the new analysis performed in 2020 (11.9 and 4.6 meq/kg, respectively).
(b): For batches NS-9127 and NS-9126, p-anisidine value, acid value and peroxide value were measured by two different external labs. Both measurements were equally performed close to production; thus, both results were reported in the table.

Table 1b: Batch to batch analysis of the NF (40% standard)

Parameter (unit)	Batch number					
	PB15232.3	PB16940715	NS-8107.2	PB19284.L	NS-9127	NS-9126
Fatty acids (%FA)						
Myristic – 14:0	0.5	0.5	0.7	0.7	0.7	0.7
Pentadecanoic – 15:0	0.1	0.1	0.1	0.3	0.1	0.1
Palmitic – 16:0	26.9	21.9	33.2	22.7	23.2	22.3
Palmitoleic – 16:1 (hexadecenoic 16:1 total)	0.2	0.3	0.2	0.3	0.3	0.3
Margaric – 17:0	0.1	0.1	0.1	0.2	0.2	0.1
Heptadecenoic – 17:1	0.2	0.3	0.2	–	0.1	0.3
Stearic – 18:0	1.8	1.5	1.5	1.5	1.4	1.3

Parameter (unit)	Batch number					
	PB15232.3	**PB16940715**	**NS-8107.2**	**PB19284.L**	**NS-9127**	**NS-9126**
Oleic – 18:1(n-9)	15.9	12.3	4.3	16.5	13.4	13
Cis-vaccenic – 18:1(n-7)	0.3	0.3	0.2	0.4	0.4	0.4
Linoleic – 18:2(n-6)	2.5	2.3	0.5	0.7	1.9	1.8
γ-Linolenic – 18:3(n-6)	0.1	0.1	0.1	0.1	0.1	0.1
α-Linolenic – 18:3(n-3)	0.1	0.2	0.1	0.1	0.1	0.2
Stearidonic –18:4(n-3)	0.1	0.2	0.2	0.2	0.2	0.2
Arachidic – 20:0	0.2	0.2	0.2	0.2	0.2	0.2
Icosenoic – 20:1 TOTAL	0.1	–	–	0.1	0.1	–
Eicosatrienoic 20:3(n-3)	–	–	–	–	–	–
Homo-γ-linolenic – 20:3(n-6)	0.1	0.1	0.2	0.1	0.1	0.2
Arachidonic – 20:4(n-6)	–	0.6	–	–	–	–
Icosatetraenoic – 20:4(n-3)	0.4	0.6	0.6	0.6	0.6	0.6
Eicosapentaenoic **(EPA)** – 20:5(n-3)	0.5	0.5	0.6	0.6	0.6	0.6
Behenic – 22:0	0.3	0.2	0.2	0.3	0.3	0.2
Docosatetraenoic – 22:4(n-6)	–	–	–	–	–	–
Docosapentaenoic (DPA) – 22:5(n-6)	7.5	9.4	10.4	8.3	9.0	10.0
Docosapentaenoic – 22:5(n-3)	0.1	0.1	0.1	0.1	0.1	0.1
Docosahexaenoic **(DHA)** – 22:6(n-3)	**40.5**	**46.3**	**44.7**	**43.5**	**44.9**	**45.3**
Tetracosanoic – 24:0	–	0.1	–	–	–	–
Minors (others in very low levels)	1.5	1.8	1.6	2.5	2.0	2.0
Free fatty acids	0.04	0.06	0.06	0.04	0.11	0.07
Trans fatty acids	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4
Sterols						
Total sterol content (mg/kg)	4,037.5	5,097.0	3,470.3	4,510.7	3,659.1	4,473.2
Cholesterol (%)	66.0	70.8	63.9	62.2	65.8	69.1
Brassicasterol (%)	2.0	2.4	3.6	3.8	3.1	2.6
Stigmasterol (%)	6.5	5.2	17.7	11	8.4	6.9
Beta-sitosterol (%)	12.8	7.4	6.6	12.1	8.7	7.6
Delta-5-avenasterol (%)	1.6	1.4	0.9	1.1	1.9	1.5
Delta-5-campesterol (%)	1.8	1.7	2.0	3.1	2.0	2.1

Parameter (unit)	Batch number					
	PB15232.3	**PB16940715**	**NS-8107.2**	**PB19284.L**	**NS-9127**	**NS-9126**
Delta-7-stigmasterol (%)	7.0	9.6	4.6	6.0	9.3	8.3
Delta-7-avenasterol (%)	2.3	1.5	0.7	0.7	0.8	1.9
Metals (mg/kg)						
Mercury	< 0.005	< 0.005	< 0.005	< 0.005	< 0.005	< 0.005
Cadmium	< 0.005	< 0.005	< 0.005	< 0.005	< 0.005	< 0.005
Arsenic	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
Lead	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
Copper	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
Iron	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
Tin	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
Aluminium	0.02	0.03	< 0.02	< 0.02	< 0.02	< 0.02
Phosphorous	< 1	-	< 1	< 1	< 1	< 1
Nickel	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
Microbiological analysis (CFU/g)						
Total plate count 30°C (ISO 4833-1)	< 10	< 40[(a)]	< 40[(a)]	< 10	< 10	< 10
Moulds	< 10	< 10	< 10	< 10	< 10	< 10
Yeasts	< 10	< 10	< 10	< 10	< 10	< 10
Coliforms 30°C (ISO 4832)	< 10	< 10	< 10	< 10	< 10	< 10
E. coli detection (ISO 16649-3)	Absence/1 g	Absence/1 g	Absence/1 g	Absence/1 g	Absence/1 g	Absence/1 g
Staphylococcus aureus detection (ISO 6888-3)	Absence/1 g	Absence/1 g	Absence/1 g	Absence/1 g	Absence/1 g	Absence/1 g
Sulfite reducing anaerobic bacteria (ISO 15213)	< 10	< 10	< 10	< 10	< 10	< 10
Bacillus cereus (ISO 7932)	< 50	< 50	< 50	< 50	< 50	< 50
Salmonella detection (real-time PCR eq. ISO 6579)	Absence/25 g	Absence/25 g	Absence/25 g	Absence/25 g	Absence/25 g	Absence/25 g
Listeria monocytogenes detection (ISO 11290-1)	Absence/25 g	Absence/25 g	Absence/25 g	Absence/25 g	Absence/25 g	Absence/25 g
Cronobacter spp detection (q PCR eq. ISO 22964)	Absent/10 g	Absent/10 g	Absent/10 g	Absent/10 g	Absent/10 g	Absent/10 g
Enterobacteria detection (ISO 21528-1)	Absent/10 g	Absent/10 g	Absent/10 g	Absent/10 g	Absent/10 g	Absent/10 g
Mycotoxins (µg/kg)						
Aflatoxin M1[(b)]	< 0.05	< 0.05	< 0.05	< 0.05	< 0.05	< 0.05
Aflatoxin B1	< 0.07	< 0.07	< 0.07	< 0.07	< 0.07	< 0.07
Aflatoxin B2	< 0.5	< 0.5	< 0.5	< 0.5	< 0.5	< 0.5

Parameter (unit)	Batch number					
	PB15232.3	PB16940715	NS-8107.2	PB19284.L	NS-9127	NS-9126
Aflatoxin G1	< 0.5	< 0.5	< 0.5	< 0.5	< 0.5	< 0.5
Aflatoxin G2	< 0.5	< 0.5	< 0.5	< 0.5	< 0.5	< 0.5
Fumonisin B1	< 1	< 1	< 1	< 1	< 1	< 1
Fumonisin B2	< 2	< 2	< 2	< 2	< 2	< 2
Fumonisin (sum of B1+B2)	< 3	< 3	< 3	< 3	< 3	< 3
T-2 Toxin	< 20	< 20	< 20	< 20	< 20	< 20
HT-2 Toxin	< 20	< 20	< 20	< 20	< 20	< 20
Nivalenol	< 200	< 200	< 200	< 200	< 200	< 200
Ochratoxin A	< 0.05	< 0.05	< 0.05	< 0.05	< 0.05	< 0.05
Patulin	< 100	< 100	< 10	< 10	< 10	< 10
Deoxynivalenol	< 5	< 5	< 5	< 5	< 5	< 5
Zearalenone	< 1	< 1	< 1	< 1	< 1	< 1
PCB and dioxins (upper bound results)						
Sum of dioxins and furans (PCDD/F TEQ) (pg/g)	0.021	0.021	0.023	0.021	0.021	0.021
Sum of dioxins, furans and dl-PCBs (total TEQ) (pg/g)	0.024	0.024	0.026	0.024	0.024	0.024
PCB (sum 6 ndl-PCBs) (ng/g)	< 0.150	< 0.150	< 0.150	< 0.150	< 0.150	< 0.150
Polycyclic aromatic hydrocarbons (µg/kg)						
Benzo[(a)]pyrene	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
Benzo[(a)]anthracene	< 0.1	< 0.1	0.2	< 0.1	< 0.1	< 0.1
Chrysene	< 0.1	< 0.1	0.1	< 0.1	< 0.1	< 0.1
Benzo[(b)]-fluoranthene	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
Sum	< 0.4	< 0.4	< 0.5	< 0.4	< 0.4	< 0.4
Pesticides						
Multiresidues GC 150	ND	ND	ND	ND	ND	ND
Multiresidues LC 150	ND	ND	ND	ND	ND	ND
Process formed contaminants						
Glycidyl fatty acid esters expressed as glycidiol (µg/kg)[(c)]	70	81	< 50	< 50	< 50	< 50
Sum of 3-MCPD and 3-MCPD fatty acid esters, expressed as 3-MCPD(µg/kg)[(d)]	214	380	< 50	< 50	< 50	< 50

Parameter (unit)	Batch number					
	PB15232.3	PB16940715	NS-8107.2	PB19284.L	NS-9127	NS-9126
Marine biotoxins						
Domoic acid (mg/kg)	NA	< 5	< 5	< 5	< 5	< 5
Okadaic acid (μg/kg)	NA	< 40	< 40	< 40	< 40	< 40
Dinophysistoxin-1 (μg/kg)	NA	< 40	< 40	< 40	< 40	< 40
Dinophysistoxin-2 (μg/kg)	NA	< 40	< 40	< 40	< 40	< 40
Pectenotoxin-2 (μg/kg)	NA	< 40	< 40	< 40	< 40	< 40
Yessotoxin (μg/kg)	NA	< 125	< 125	< 125	< 125	< 125
Homo yessotoxin (μg/kg)	NA	< 125	< 125	< 125	< 125	< 125
Azaspiracid-1 (μg/kg)	NA	< 40	< 40	< 40	< 40	< 40
Azaspiracid-2 (μg/kg)	NA	< 40	< 40	< 40	< 40	< 40
Azaspiracid-3 (μg/kg)	NA	< 40	< 40	< 40	< 40	< 40
13-desmethyl spirolide C (μg/kg)	NA	< 100	< 100	< 100	< 100	< 100
Gymnodimine (μg/kg)	NA	< 50	< 50	< 50	< 50	< 50
Pinnatoxin G (μg/kg)	NA	< 25	< 25	< 25	< 25	< 25

NA: not analysed; ND: Not detected; 3-MCPD: 3-monochloro-propanol-1,2-diol.
(a): Total plate count at 30°C was detected but at levels lower than 40 CFU/g.
(b): It is noted that aflatoxin M1 in infant formulae (IF) should not exceed 0.025 μg/kg while an LOQ of 0.05 μg/kg was used to perform the analysis. Nevertheless, considering the incorporation rate of the NF in IF (max 87.5 mg NF/100 mL), the limit of 0.025 μg/kg in IF is expected to be respected.
(c): It is noted that glycidyl fatty acid esters in infant formulae (IF) should not exceed the maximum level (ML) of 6 μg/kg for liquid IF and FOF while a max concentration of 81 μg/kg was found in batch PB16940715. However, considering the incorporation rate of the NF in IF (max 87.5 mg NF/100 mL), the ML of 6 μg/kg in IF is expected to be respected.
(d): It is noted that the sum of 3-MCPD and 3-MCPD esters, expressed as free 3-MCPD in IF should not exceed the maximum level (ML) of 15 μg/kg for liquid IF and FOF while a max concentration of 380 μg/kg (sum expressed as 3-MCPD) was found in batch PB16940715. However, considering the incorporation rate of the NF in IF (max 87.5 mg NF/100 mL), the ML of 15 μg/kg in IF is expected to be respected.

3.4.1. Stability

Stability of the NF (*Schizochytrium* sp. oil) during storage

The applicant recommends storing the oil under frozen conditions (–18°C) for not more than 2 years, to guarantee the properties of the product. Alternatively, a storage duration of 6 months at –15°C may also be suitable according to the applicant. The applicant recommends storage in sealed steel drums that are flushed with nitrogen to limit the oxygen availability. To support these recommendations, the applicant has provided a stability study.

In this study, the laboratory made use of representative batches of the NF, which were produced 24 and 43 months before being analysed and stored under frozen conditions at temperature of –20°C and –24°C. This range of temperature is expected to ensure the maximum temperature of –18°C is not exceeded in practice. Two independent batches of the NF (40% S) were analysed for the two chemical stability parameters generally measured to follow the oxidation of oils: the peroxide index and the p-anisidine value. Additional analyses were also performed on the 40% and 50% winterised formulations of the NF, but only 40% S results are reported in detail because this is the relevant formulation of the NF.

Results were compared with the levels found in the freshly produced samples (measurement at time 0). In addition, the measured peroxide index and the p-anisidine value were compared with the specification currently on the Union list (peroxide index: 5 meqO_2/kg) and with the usual standards for p-anisidine value.[6]

The peroxide index was found to remain within the specifications (≤ 5 meqO_2/kg) when samples were stored under proposed conditions of 2 years at –18°C, or even after a longer storage period of 43 months. It is noted that measurements performed on 40% W and 50% W formulations of the NF also confirmed these findings. Regarding the p-anisidine value, the maximum value observed after storage at –18°C was 8.1 (batch 1 at 24 months). Therefore, it remained below 10 under the proposed conditions of storage.

Table 2: Peroxide index and p-anisidine value in the stability study (storage condition –18°C)

Time (in months)		0	24	43
Peroxide index (meqO_2/kg)	Batch 1 (40% S)	0	1.6	–
	Batch 2 (40% S)	0.9	–	2.9
p-anisidine value	Batch 1 (40% S)	5.9	8.1	–
	Batch 2 (40% S)	5.5	–	5.5

The storage stability study confirmed that the proposed conditions of storage of the NF (maximum 2 years, deep frozen in sealed steel drums drums flushed with nitrogen) are sufficient to avoid oxidative degradation of the NF. Furthermore, considering that the conditions of storage prevent contact of the NF with moisture, heat, light and enzyme activity, hydrolytic degradation and/or microbiological contamination of the NF is not expected to occur under the recommended storage conditions. Consequently, the Panel considers that the data provided sufficient information with respect to the stability of the NF during storage of 24 months.

Stability under the intended conditions of use (i.e. when the NF oil is powdered to be incorporated to infant formulae and follow-on formulae)

According to the conditions of use proposed by the applicant, the NF is intended to be incorporated (as a food ingredient) into infant formulae and follow-on formulae. The NF may undergo further processing steps (e.g. dry powdering) before being incorporated in infant formulae and follow-on formulae. The stability of the NF ingredient when undergoing such processing was investigated by the applicant by means of analytical stability tests and sensory stability tests.

Analytical tests:

A batch of NF (40% S formulation) has been transformed to a dried powder by microencapsulation by microencapsulation to simulate a product suitable for use in infant formulae. The powder has then been flushed with nitrogen and stored for 11 months at +20°C. The applicant has reported analytical results for oxidation indicators (peroxide index and p-anisidine value) and for DHA content measured

[6] The European Pharmacopoeia defines a p-anisidine value of maximum 10 for cod liver and salmon oil. This limit can be extrapolated to *Schizochytrium* sp. oil. In the US Pharmacopoeia, the limit value is 20 for *Schizochytrium* oil (source: https://onlinelibrary.wiley.com/doi/full/10.1002/lite.201600013).

in the 'oil sample' (the NF before powdering), in 'Powder sample T0' (powdered NF just after treatment), and in 'Powder sample T11' (powdered NF after 11 months of storage). It is noted that the process for obtaining the measurements for the powdered samples involved extraction of the oil from the powder to determine the oxidation indicators and DHA content. All analyses were conducted in external laboratories for which Certificates of Accreditations were provided. A summary of the results is reported in the Table 3.

Table 3: Peroxide index, p-anisidine value and DHA concentration in the NF before and after powdering, and after 11 months of storage

Parameter	Oil sample (NF)[(a)]	Parameter	Powder sample	
			T0[(b)]	T11[(c)]
Peroxide index ($meqO_2/kg$)	0.0	Peroxide index ($meqO_2/kg$)	< 0.3	0.0
p-anisidine value	5.9	p-anisidine value	n.a.	4.5
–	–	DHA% in powder (as TG)	12.4	11.7
–	–	FA% in powder (as TG)	29	27.5
DHA% (g DHA/100 g FA) DHA% (g FA/100 g oil)	46.3 43.02	DHA% (g DHA/100 g FA)[(d)]	42.8	42.5

n.a.: not available; DHA: docosahexaenoic acid; FA: fatty acid; TG: triglycerides; calc: calculated.
(a): Sample of the NF under its oily form, as produced by the applicant (Batch No. PB16940715.L-N40 in Tables 1a and 1b).
(b): Powder form of the NF just after processing.
(c): Powder form of the NF after 11 months of storage at +20°C under nitrogen atmosphere.
(d): Indicative ratio calculated as [DHA% in the powder (as TG)]/[FA% in powder (as TG)].

These results show that both peroxide index and p-anisidine values remain stable after the powdering process and further storage of the powder. This indicates that the conditions of use would not induce a critical oxidative degradation of the NF. It was noted that the absolute DHA content in the powder (11.7–12.4%) is lower compared to the NF (> 40%). This is because the FA content in the powder (28–29%) is much lower than in the NF (> 98%) due to the emulsion recipe of the powder. On a fatty acid basis, the powdering step and the storage did not significantly alter the DHA content of the NF under the intended conditions of use.

Sensory tests:

The applicant has also reported a sensory stability study. In this study, the laboratory tested the storage of a powder formulation in which DHA (from the NF) had previously been incorporated. This powder is referred to as 'milk-based protein encapsulates' containing DHA and is the usual form of the DHA products ready for use as an ingredient of infant formula. Accelerated shelf-life tests were performed on the solid powder (containing 10% DHA). Three different storage conditions were tested: storage period of 12 weeks (at 30°C, air atmosphere), 18 weeks (at 30°C, N_2-protected atmosphere) and 12 months (at 20°C, N_2-protected atmosphere).

After storage, the samples were diluted in warm milk following the normal conditions of use and the organoleptic parameters (taste, flavour, colour) of the reconstituted milk were scored by a trained panel.[7] The applicant suggests that qualitative degradation of the product (e.g. oxidation of the oil) can be noticed by the trained panel because oxidation of DHA-rich oils generally induces a strong marine/fishy smell and taste. Based on predefined qualitative criteria (appearance and notes of fish, sweet/Maillard, musty, oxidation, acidity/sharp, soapy, bitter and salt/briny), the trained panel scored the different samples using a 5-point scale. This test as well as the scoring system was developed in-house to assess the quality of the product. Overall, the sensory score of all samples was found to be above the acceptance level defined in the test, in all tested conditions. This study is deemed supportive only.

Given the results of the analytical tests and the supportive information of the sensory test, the Panel considers that the data provided sufficient information with respect to the stability of the NF under the proposed conditions of use.

[7] From a trained sensory panel pool of 20 panel members, approximately five members were selected to perform the sensory evaluation of the powder samples.

3.5. Specifications

As the NF '*Schizochytrium* sp. oil' is already authorised on the EU market, specifications for this NF are currently presented in the Union list. The Panel verified whether the NF under assessment complies with these specifications and subsequently assessed the need to define further specifications for the NF under assessment.

Current specifications of the NF (Union list)

Parameters and corresponding values of the current specifications for the '*Schizochytrium* sp. oil' are reported in Table 4. It is noted that the NF currently authorised is not strain specific. Furthermore, the NF under assessment is currently used as a source for the authorised novel food '*Schizochytrium* sp. oil'. Therefore, the NF under assessment shall comply with the specifications currently defined for '*Schizochytrium* sp. oil'. A comparison with the data from the batch to batch analysis of the present NF is presented in Table 4.

According to the data submitted in the present dossier, the NF produced by the applicant complies with the current specifications. The maximum values observed in the batch to batch analysis for the acid value, peroxide value, moisture and volatiles, unsaponifiable and trans-fatty acids are below the limits defined in the specifications (see Table 4). The results of the storage stability studies indicated that the specifications are also met when the NF is stored under the proposed conditions of storage (see Section 3.4.1).

Table 4: Specifications of the NF (as currently reported in the Union list) and comparison with analytical content of the NF under assessment

Parameter	Specification for *Schizochytrium* sp. oil (union list)	NF under assessment (based on batch to batch analysis)	Method of analysis
Acid value (mg KOH/g)	≤ 0.5	0.28 (max)	Not reported[(a)]
Peroxide value (meqO2/kg)	≤ 5.0	4.8 (max)	Not reported[(a)]
Moisture and volatile (%)	≤ 0.05	0.02 (max)	Not reported[(a)]
Unsaponifiables (%)	≤ 4.5	1.29 (max)	Not reported[(a)]
Trans-fatty acids (%)	≤ 1.0	< 0.4	Not reported[(a)]
DHA-content (%)	≥ 32.0	40.5–46.3	Not reported[(a)]

(a): Method of analysis is not reported on the Union list.

The NF under assessment complies with the specifications for '*Schizochytrium* sp. oil' that is already authorised on the EU market.

Discussion on additional specifications for the uses assessed in the present dossier

The applicant used a strain of *Schizochytrium* sp. (strain WZU477) in the production of the NF and this strain impacts on the FA profile of the NF. Notably, concentrations of DHA range between 40.5% and 46.3% of fatty acids content while the minimum required by the specifications is 32%. Therefore, the applicant proposes to amend the current specifications of the Union list to consider this particularity of the NF. The Panel considers that amending the specification to modify the minimum concentrations of DHA (e.g. > 40% instead of 32%) is not necessary from a safety point of view.

The applicant wishes to specify that on the Union list, the authorised uses in IF and FOF are only valid when the NF '*Schizochytrium* sp. oil' is produced from strain WZU477. It was demonstrated that this strain belongs to the species *Schizochytrium limacinum* and the Panel has considered key information on this species to conclude on the safety of the production process. However, the Panel did not consider data that are specific to the strain WZU477. A risk management decision needs to be taken whether the strain WZU477 should be reported in the specifications for the NF '*Schizochytrium* sp. oil'. The Panel notes that for the NFs *Schizochytrium* sp. (ATCC PTA-9695) oil and *Schizochytrium* sp. (T18) oil), which are currently on the Union list and authorised in IF and FOF, the strain is mentioned in the name of the NF. However, these two strains (ATCC PTA 9695 and T18) were not identified at species level in the Union list because this information was not used in the risk assessment. The risk assessment for these two NFs was based on specific toxicity studies.[8]

[8] The NFs *Schizochytrium* sp. (ATCC PTA-9695) oil and *Schizochytrium* sp. (T18) oil were assessed independently as separate NFs. Specific toxicological studies performed with these NFs were considered to assess these NFs.

It is noted that the safety assessment of the NF for its use in IF and FOF required a detailed analysis of potential contaminants. Most of them are covered by sectoral legislation (e.g. Regulation on infant formulae). For marine biotoxins, however, risk managers may consider amending the specifications for the NF '*Schizochytrium* sp. oil' when authorised in IF and FOF in order to set the limits at the LOQ achieved in the batch to batch analysis.

The Panel notes that the p-anisidine value, which allows monitoring the secondary oxidation of oils, has not been considered so far on the Union list for *Schizochytrium* oils. However, secondary oxidation products (such as α,β-unsaturated carbonyl compounds, malonaldehyde) may be of safety concern (Vieira et al., 2017; Kanner, 2007). Therefore, the Panel proposes to add the p-anisidine value in the specifications for *Schizochytrium* sp. oils. Considering the European Pharmacopoeia values defined for cod liver and salmon oils (2015) and the compositional data, a limit of 10 could be used for the p-anisidine value in *Schizochytrium* oils.

3.6. History of use of the NF and/or of its source

3.6.1. History of use of the source

The source of the NF is a microalga belonging to the genus *Schizochytrium* (see full description in Section 3.2). This genus has been used as a source of DHA-rich oils since 2003, year of the first authorisation of the NF DHA-rich oil from *Schizochytrium* (Commission Decision 2003/427/EC[9]). The first assessment of DHA-rich oil from *Schizochytrium* sp. was referring to the strain ATCC 2088 (United Kingdom, 2002). However, several other strains have been recognised as valid sources for this NF since 2003.

The NF under assessment is produced by the strain WZU477 (see Section 3.2). Following a substantial equivalence dossier assessed in the Netherlands by the Committee on Safety Assessment of Novel Foods (VNV Committee) (CBG-Meb, 2014), the production strain WZU477 was recognised as a valid source to produce a DHA-rich oil equivalent to the original NF. DHA-rich oils produced from strain WZU477 are therefore covered by the generic NF *Schizochytrium* sp. oil already reported on the Union list. It is noted that these oils are currently not allowed to be added to IF and FOF.

Since 2015, two other strains belonging to the genus *Schizochytrium* were also approved for the production of DHA-rich oils: strain ATCC PTA-9695 (2015) and strain T18 (2017). These two strains are specifically mentioned on the Union list as part of the name of two separate NF entries. Furthermore, the NFs '*Schizochytrium* sp. (T18) oil' and '*Schizochytrium* sp. (ATCC PTA-9695) oil' were also authorised in IF and FOF. These are currently the only DHA oils from *Schizochytrium* authorised for use in infant and follow-on formulae.

3.6.2. History of use of the NF

DHA-rich oils from *Schizochytrium* have been on the EU market since 2003. On the Union list, there are currently four different entries referring to *Schizochytrium* DHA-rich oils.

Table 5: Overview of the NFs based on Schizochytrium DHA-rich oil currently present in the Union List

Name of the novel food	Year of 1st authorisation	Decisions	Remarks
Schizochytrium sp. oil	2003	Decision 2003/427/EC[(a)], 2009/778/EC[(b)], 2014/463/EU[(c)] and 2019/109[(d)]	Extension of use under assessment for IF and FOF (so far not authorised for this NF)
Schizochytrium sp. oil rich in DHA and EPA	2012	Authorised by United Kingdom	–
Schizochytrium sp. (ATCC PTA-9695) oil	2015	Decision 2015/545[(e)]	Authorised use on IF and FOF
Schizochytrium sp. (T18) oil	2017	Authorised by Ireland	Authorised use on IF and FOF

[9] Commission Decision 2003/427/EC: Commission Decision of 5 June 2003 authorising the placing on the market of oil rich in DHA (docosahexaenoic acid) from the microalgae *Schizochytrium* sp. as a novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council. OJ L 144, 16.6.2003, p. 13–14.

(a): Commission Decision 2003/427/EC: Commission Decision of 5 June 2003 authorising the placing on the market of oil rich in DHA (docosahexaenoic acid) from the microalgae *Schizochytrium* sp. as a novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council. OJ L 144, 16.6.2003, p. 13–14.
(b): Commission Decision 2009/778/EC: Commission Decision of 22 October 2009 concerning the extension of uses of algal oil from the micro-algae Schizochytrium sp. as a novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council. OJ L 278, 23.10.2009, p. 56–57.
(c): Commission Implementing Decision 2014/463/EU: Commission Implementing Decision of 14 July 2014 on authorising the placing on the market of oil from the micro-algae Schizochytrium sp. as a novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council and repealing Decisions 2003/427/EC and 2009/778/EC. OJ L 209, 16.7.2014, p. 55–58.
(d): Commission Implementing Regulation (EU) 2019/109 of 24 January 2019 authorising an extension of use of Schizochytrium sp. oil as a novel food under Regulation (EU) 2015/2283 of the European Parliament and of the Council, and amending Commission Implementing Regulation (EU) 2017/2470. OJ L23, 25.1.2019, p. 7–10.
(e): Commission Implementing Decision (EU) 2015/545 of 31 March 2015 authorising the placing on the market of oil from the micro-algae Schizochytrium sp. (ATCC PTA-9695) as a novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council; OJ L 90, 2.4.2015, p. 7–10.

The application under assessment is an extension of use for the first NF, referred to as generic *Schizochytrium* sp. oil. This NF has been authorised since 2003 by means of Commission Decision 2003/427/EC[9]. It has been subject to several extensions of use which were reported in Commission Decision 2009/778/EC[10], Commission Implementing Decision 2014/463/EU[11] and Commission Implementing Regulation 2019/109[12]. The NF *Schizochytrium* sp. oil is currently authorised as a food supplement (250 mg/day for the general population; 450 mg/day for pregnant and lactating women) and as a food ingredient in a wide range of food categories (use levels are expressed in mg of DHA): Milk-based drinks and similar products intended for young children (200 mg/100 g); processed cereals-based food and baby foods for infants and young children (200 mg/100 g); food intended to meet the expenditure of intense muscular effort (200 mg/100 g); food bearing statements on the absence or reduced presence of gluten (200 mg/100 g); food for specific medical purposes; bakery products (breads, rolls and sweet biscuits) (200 mg/100 g); cereal bars (500 mg/100 g); breakfast cereals (500 mg/100 g); cooking fats (360 mg/100 g); dairy analogues except drinks (200–600 mg/100 g); dairy products except milk-based drinks (200–600 mg/100 g); non-alcoholic beverages (including dairy analogue and milk-based drinks) (80 mg/100 mL); spreadable fats and dressings (600 mg/100 g). An extension of use has recently been granted for fruit and vegetables puree (100 mg/100 g).

Besides the generic NF *Schizochytrium* sp. oil under assessment, three other NFs are also present on the Union list: *Schizochytrium* sp. oil rich in DHA and EPA; *Schizochytrium* sp. (ATCC PTA-9695) oil and *Schizochytrium* sp. (T18) oil. These NFs were authorised for the same food categories as the generic NF *Schizochytrium* sp. oil reported above, plus some additional uses. In particular, the two strain-specific NFs *Schizochytrium* sp. (ATCC PTA-9695) oil and *Schizochytrium* sp. (T18) oil were authorised for use in IF and FOF. These NFs can be used in accordance with Regulation (EU) 609/2013[13], which was supplemented by Regulation (EU) 2016/127[14].

Consequently, the use of DHA-rich oil from *Schizochytrium* in infant formulae and follow-on formulae is currently authorised but is strictly restricted to DHA-rich oils produced from two specific strains of *Schizochytrium*: ATCC PTA-9695 and T18.

[10] Commission Decision 2009/778/EC: Commission Decision of 22 October 2009 concerning the extension of uses of algal oil from the micro-algae Schizochytrium sp. as a novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council. OJ L 278, 23.10.2009, p. 56–57.
[11] Commission Implementing Decision 2014/463/EU: Commission Implementing Decision of 14 July 2014 on authorising the placing on the market of oil from the micro-algae Schizochytrium sp. as a novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council and repealing Decisions 2003/427/EC and 2009/778/EC. OJ L 209, 16.7.2014, p. 55–58.
[12] Commission Implementing Regulation (EU) 2019/109 of 24 January 2019 authorising an extension of use of Schizochytrium sp. oil as a novel food under Regulation (EU) 2015/2283 of the European Parliament and of the Council, and amending Commission Implementing Regulation (EU) 2017/2470. OJ L23, 25.1.2019, p. 7–10.
[13] Regulation (EU) No 609/2013 of the European Parliament and of the Council of 12 June 2013 on food intended for infants and young children, food for special medical purposes and total diet replacement for weight control and repealing Council Directive 92/52/EEC, Commission Directives 96/8/EC, 1999/21/EC, 2006/125/EC and 2006/141/EC, Directive 2009/39/EC of the European Parliament and of the Council and Commission Regulations (EC) No 41/2009 and (EC) No 953/2009 Text with EEA relevance; OJ L 181, 29.6.2013, p. 35–56.
[14] Commission Delegated Regulation (EU) 2016/127 of 25 September 2015 supplementing Regulation (EU) No 609/2013 of the European Parliament and of the Council as regards the specific compositional and information requirements for infant formula and follow-on formula and as regards requirements on information relating to infant and young child feeding; OJ L 25, 2.2.2016, p. 1–29.

3.7. Proposed uses and use levels and anticipated intake

3.7.1. Target population

The NF is intended to be added to infant formula (IF) and follow-on formula (FOF). Consequently, the target population defined by the applicant is infants and young children.

3.7.2. Proposed uses and use levels

The NF is intended to be added to IF and FOF. The applicant derived the use level directly from Regulation (EU) 2016/127, which defines the specific compositional and information requirements for IF and FOF. Based on the EFSA opinion on recommendations for composition of IF and FOF (EFSA, 2014a), Regulation (EU) 2016/127 states the mandatory addition of DHA to IF and FOF at levels ranging between 4.8 and 12 mg/100 kJ (eq. 20–50 mg/100 kcal). Considering a standard energy content of maximum 70 kcal per 100 mL of IF/FOF defined in Regulation (EU) 2016/127, the DHA level in the reconstituted formula is expected to range between 14 and 35 mg DHA/100 mL.

Considering that the concentration of DHA in the NF is minimum 40%, the applicant defined a use level for the NF of 35–87.5 mg NF/100 mL, to reach the target of 14–35 mg DHA/100 mL. It should be noted that manufacturers of IF and FOF who may powder the NF and incorporate it into their formulae shall guarantee that the concentration of DHA meets the requirement of the Regulation. This is also the case if other sources of DHA are used in combination with the NF.

3.7.3. Anticipated intake of the NF

As the use level proposed by the applicant is directly derived from Regulation (EU) 2016/127 (see Section 3.7.2), the intake of DHA for infants fed with IF supplemented with the NF at the proposed use level is within the range foreseen by the Regulation.

The Panel assessed the maximum intake of NF resulting from the use of the NF in IF. The conservative scenario where IF is the only food consumed by non-breastfed infants from 0 to 4 months was considered, using the default value of 260 mL/kg body weight (bw) per day for high formula intakes for infants 0–4 months (EFSA Scientific Committee, 2017). Based on the use level defined by the applicant (maximum concentration of NF in IF of 87.5 mg/100 mL), the high intake of NF resulting from the consumption of IF is estimated to be 227.5 mg NF/kg bw per day.[15] Considering that 40% of the NF is DHA, the estimated high daily intake of DHA from IF is 91 mg/kg bw per day.

Furthermore, two other DHA-rich oils from *Schizochytrium*[16] are currently already authorised for use in IF and FOF, with use levels also in line with Regulation (EU) 2016/127. Consequently, the intended use of IF and FOF currently under assessment for the NF *Schizochytrium* sp. oil (from strain WZU477) is not expected to modify the current daily intake of DHA-rich oil for infants and young children. The NF is proposed as an alternative source of DHA for IF and FOF.

3.8. Absorption, distribution, metabolism and excretion (ADME)

The applicant did not submit specific ADME data for the NF and such data are not deemed necessary. The digestion, absorption and metabolism of DHA have been extensively documented in the EFSA Scientific Opinion on tolerable upper intake level of EPA, DHA and DPA (EFSA NDA Panel, 2012).

3.9. Nutritional information

The nutritional content of the NF is provided by the batch to batch analysis. The NF mainly consists of fat in the form of triglycerides. Trans-fatty acids were not detected, and based on the acid value, free FA are not expected to be of concern. The FA profile reveals that DHA is the predominant compound. DHA is an essential nutrient for infants and children. The essential role of DHA for the development of infant and young children (e.g. nervous system and the retina) has been documented in the EFSA Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union (EFSA NDA Panel, 2013). When used in accordance with the proposed

[15] The mean body weight of a 0- to 3-month infant is 5 kg and is used as a default body weight for the whole group of infants (EFSA Scientific Committee, 2012).

[16] *Schizochytrium* sp. (ATCC PTA-9695) oil and *Schizochytrium* sp. (T18) (see Section 3.6.2).

use level, the NF can enrich the composition of IF and FOF to such extent that the latter fall within the range targeted by the current Regulation (20–50 mg DHA/100 kcal).

The concentrations of sterols found in the NF are around 3,000–5,000 mg/kg fat. However, given that the NF will be incorporated into IF and FOF at a maximum rate of 87.5 mg NF/100 mL, the actual contents of sterols in IF and FOF are not considered to be of health concern.

In general, the analysis of the FA profile of the NF shows the presence of other components which might affect the overall ratio of FA in IF and FOF. However, it falls under the responsibility of the manufacturers to guarantee that the overall ratio of FA complies with the current regulations.

The Panel considers that taking into account the composition of the NF and the proposed conditions of use, consumption of the NF is not nutritionally disadvantageous.

3.10. Toxicological information

3.10.1. Qualified presumption of safety (QPS)

The available evidence indicates that the source organism (*Schizochytrium* sp., strain WZU477) belongs to the species *Schizochytrium limacinum*. In 2020, *Schizochytrium limacinum* was assessed by the EFSA Panel on Biological Hazards (BIOHAZ) for its suitability to be added to the list of QPS-recommended biological agents intentionally added to food or feed. In the opinion of BIOHAZ Panel, *Schizochytrium limacinum* was identified as a synonym of *Aurantiochytrium limacinum.* The BIOHAZ Panel considered the identity, the body of knowledge and potential safety concerns of this microorganism. The literature searches performed did not provide any evidence for a safety concern for human or animal health for any use of *S. limacinum*. The BIOHAZ Panel concluded that *S. limacinum* may be recommended for the QPS list with the qualification 'for production purposes only' (EFSA BIOHAZ Panel, 2020).

3.10.2. Absence of marine biotoxins

The absence of marine biotoxins was demonstrated in the assessment of the composition of the NF (see Section 3.4). The Panel verified whether the LOQs used in the reported analysis of the common marine biotoxins were sufficiently low compared to the acute reference dose (ARfD) of the respective biotoxins (EFSA CONTAM Panel, 2009). It was found that the theoretical intakes resulting from the occurrence of marine biotoxins at their respective LOQs remain well below the respective ARfD of the corresponding biotoxins (see Table 6). It is concluded that the reported LOQs are sufficiently low to ensure consumer safety. Consequently, they can be considered in the specifications.

Table 6: Theoretical exposure to marine biotoxins considering the LOQs and comparison with the respective acute reference doses (ARfD)

Marine biotoxin	LOQ[(a)]	Theoretical maximal biotoxin intake expressed in μg/kg bw per day[(b)]	ARfD[(c)] (μg/kg bw)	ARfD/Theoretical biotoxin intake
Azaspiracids	40 μg/kg	0.0091	0.2	22
Pectenotoxins	40 μg/kg	0.0091	0.8	88
Yessotoxins	125 μg/kg	0.0284	25	879
Amnesic shellfish toxin, domoic acid	5 mg/kg	1.1375	30	26
Paralytic shellfish toxin, saxitoxin	n.r.	–	0.5	–
Okadaic acid	40 μg/kg	0.0091	0.3	33

LOQ: Limit of Quantification ARfD: Acute reference dose; n.r.: not reported.
(a): Limit of Quantification reached in the compositional analysis of the NF (see Section 3.4).
(b): Considering the critical exposure of non-breastfed infant resulting in 227.5 mg NF/kg bw per day and respective LOQs of biotoxins.
(c): Acute reference dose assessed in EFSA CONTAM Panel (2009).

3.10.3. Toxicity of DHA oils derived from *Schizochytrium sp*

No toxicity studies that were conducted with the novel food under assessment (DHA-rich oil produced from strain WZU477 of *Schizochytrium sp*.) have been provided.

However, the toxicity of DHA-rich algal oils produced from different strains of *Schizochytrium sp.* has been well documented over the last decades. Several guideline compliant studies, including bacterial reverse mutation tests, *in vitro* chromosomal aberration tests, *in vivo* mammalian cell micronucleus tests, subchronic toxicity studies with rats and developmental and reproductive toxicity studies with rats, were performed with various forms of DHA algal oils from *Schizochytrium sp.* Most of these studies were assessed and used to conclude on the safety of NFs evaluated in former authorisation frameworks. Notably two studies performed with DHA oil produced from strain ATCC PTA-9695 (Fedorova-Dahms et al., 2011 and an unpublished study) were performed to support the authorisation of the NF *Schizochytrium* sp. (ATCC PTA-9695) in infant and follow-on formula. These studies have been assessed by the UK competent authority in 2014 (United Kingdom, 2014). Similarly, two other studies performed with DHA oil produced from strain T18 (Schmitt et al., 2012a,b) have also been considered by the UK competent authority in support of the authorisation of the NF Schizochytrium sp. (T18) in infant and follow-on formula in 2017 (United Kingdom, 2017). In addition, two other studies (Lewis et al., 2016; Falk et al., 2017), performed with DHA oils from unspecified strains of *Schizochytrium sp.,* have been considered in the assessment of Anses (2018).

In all previous assessments, the competent authorities concluded that there were no concerns with regard to genotoxicity and subchronic toxicity of the tested materials. Further studies found in the literature indicate the same outcome for a diversity of DHA oils produced from other strains of *Schizochytrium sp.* which have a longer history of use (Hammond et al., 2001a, 2001b, 2002; Blum et al., 2007; Kroes et al., 2003; Abril et al., 2003).

3.10.4. Summary

Even though toxicological tests were not conducted with the NF that is assessed in the present opinion, the Panel considers that, given the results on toxicity in studies performed with various forms of DHA oils derived from *Schizochytrium sp.*, given the QPS status of the source of the NF and considering data on the production process and on the composition of the NF (absence of viable cells, absence of marine biotoxins), there are no concerns with regard to toxicity of the NF.

3.11. Allergenicity

The applicant provided a proximate analysis of the NF, which indicates that proteins were below the LOQ (0.01 g/kg). The Panel considers that the NF is unlikely to trigger adverse allergic reactions in the general population or subgroups thereof under the proposed conditions of use.

4. Discussion

The NF, which is the subject of the application, is a DHA-rich oil derived from *Schizochytrium* sp. (strain WZU477). The available evidence indicates that the source organism (*Schizochytrium* sp., strain WZU477) belongs to the species *Schizochytrium limacinum*. The Panel considers that the information provided on the composition of the NF is sufficient and does not raise safety concerns.

In 2020, *Schizochytrium limacinum* was assessed by the EFSA BIOHAZ Panel and attributed the QPS status with the qualification 'for production purposes', which implies the absence of viable *Schizochytrium* cells in the final product. The NDA Panel considers that based on the information provided on the production process, the microalga is not expected to survive the manufacturing process. The Panel considers that the production process is sufficiently described and does not raise safety concerns.

The applicant intends to market the NF as an ingredient for IF and FOF to meet the requirement of Regulation (EU) 2016/127. Consequently, the proposed use levels (defined on DHA basis) are the same as for the other DHA-rich oils from *Schizochytrium* sp. which are currently on the market and authorised for supplementing DHA in IF and FOF. Therefore, the intake of DHA resulting from the proposed use is not expected to modify the current situation as regards the total intake of DHA in infants and young children.

Toxicological tests conducted with the NF were not performed. However, based on the available toxicological data on various forms of DHA oils derived from *Schizochytrium* sp., the QPS status of the source of the NF, the production process and the composition of the NF (absence of viable cells, absence of marine biotoxins), the Panel considers that there are no concerns with regard to toxicity of the NF.

5. Conclusions

The Panel concludes that the NF, i.e. *Schizochytrium sp.* oil (produced from the strain WZU477 belonging to species *Schizochytrium limacinum*), is safe under the proposed conditions of use. The target population is infants and young children.

The Panel could not have reached the conclusion on the safety of the NF under the proposed conditions of use without the following data claimed as proprietary by the applicant:

- Original submitted data: Annex I (NF application 2012); detailed description of the production process; Annex II (chemical characteristics); Annex III (fatty acid analysis); Annex IV (sterol analysis); Annex V (heavy metals analysis); Annex VI (PAH analysis); Annex VII (mycotoxin analysis); Annex VIII (dioxin, dioxin like, PCB, pesticides analysis); Annex IX (microbiological analysis); Annex XI (retrospective stability study); Annex XII (analytical lab certificates); Appendix B.2 (compositional data NF);
- Additional submitted data: Annex IV (protein analysis); Annex VI (3 MCPD & glycidyl ester analyses); Annex VII (physicochemical analysis); Annex VIII (microbiological analysis); Annex IX (heavy metals analysis); Annex X (mycotoxin analysis); Annex XI (PAH, dioxin and dioxin-like contaminants analysis); Annex XII (fatty acid profile analysis); Annex XIV (sterol composition analysis); Annex XVII (hydrolytic rancidity analysis over time); Annex 1 (marine biotoxin analysis); Annex 3 (stability study); Annex I (certificate of analysis).

6. Steps taken by EFSA

1) Letter from the European Commission to the European Food Safety Authority with the request for a scientific opinion on the safety of *Schizochytrium* sp. oil as a novel food Ref. Ares(2019)4000797, dated 24 June 2019.
2) On 24/06/2019, a valid application on *Schizochytrium* sp. oil as a novel food, which was submitted by Progress Biotech bv, was made available to EFSA by the European Commission through the Commission e-submission portal (NF 2019/0983) and the scientific evaluation procedure was initiated.
3) On 18/11/2019, EFSA requested the applicant to provide additional information to accompany the application and the scientific evaluation was suspended.
4) On 19/06/2020, additional information was provided by the applicant and the scientific evaluation was restarted.
5) During its meeting on 31 August 2020, the NDA Panel, having evaluated the data, adopted a scientific opinion on the safety of *Schizochytrium* sp. oil as a NF pursuant to Regulation (EU) 2015/2283.

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Abbreviations

ADME	absorption, distribution, metabolism and excretion
AI	Adequate intake
ALA	alpha linolenic acid
ARfD	Acute Reference Dose
ATCC	American Type Culture Collection
BIOHAZ	Panel on Biohazards
Bw	body weight
CFU	Colony-forming unit
DHA	docosahexaenoic acid
DNA	deoxyribonucleic acid
DPA	docosapentaenoic acid
EPA	eicosapentaenoic acid
FA	fatty acids
FOF	follow-on formula
GMP	Good Manufacturing Practice
HACCP	Hazard Analysis Critical Control Points
IF	infant formula
ISO	International organization for standardization
LOQ	limit of quantification
MCPD	Monochloro-propanol-1,2-diol
ML	Maximum level
NDA	Panel on Nutrition, Novel Foods and Food Allergens
NF	novel food
PCB	Polychlorobiphényles
PCR	Polymerase Chain Reaction
PUFA	polyunsaturated fatty acids
QPS	qualified presumption of safety
rDNA	ribosomal DNA
rRNA	ribosomal RNA
TG	Triglyceride
TEQ	Toxicological equivalency
UK	United Kingdom
VNV	Committee on Safety Assessment of Novel Foods